KW:mmw072501/9241053A.PAMD

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Applicant	:	James C. Costin
Serial No.	:	New Divisional Application (From S/N 09/265,640, Filed 03/10/99)
Filed	:	Herewith
For	:	METHOD AND COMPOSITION FOR THE ERADICATION AND CONTROL OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS BACTERIA AND THE PREVENTION OF ANTIBIOTIC DRUG RESISTANCE IN SAID BACTERIA
Examiner	:	E. White
Art Unit	:	1623
Attorney Docket No.	:	924.1.053A

EXPRESS MAIL CERTIFICATE
DATE July 25, 2001
LABEL NO. EL 488122413 US
I HEREBY CERTIFY THAT, ON THE DATE INDICATED ABOVE, I DEPOSITED THIS PAPER OR FEE WITH THE U.S. POSTAL SERVICE AND THAT IT WAS ADDRESSED FOR DELIVERY TO THE COMMISSIONER OF PATENTS & TRADEMARKS, WASHINGTON, DC 20231 BY "EXPRESS MAIL POST OFFICE TO ADDRESSEE" SERVICE
NAME (PRINT) Mandy Willever
SIGNATURE Mandy Willever

Commissioner of Patents
Washington, D.C. 20231

July 25, 2001

PRELIMINARY AMENDMENT

Dear Sir:

Please calculate the fee after entry of this Preliminary Amendment.

This Divisional Application is herewith filed in response to the Office Action of June 1, 2001 in co-pending parent Application Serial No. 09/265,640. A "Petition For Extension Of Time" has been filed in parent Application Serial No. 09/265,640, for extending the time to reply to the aforesaid Office Action to August 1, 2001.

IN THE ABSTRACT:

Change the ABSTRACT to the clean version provided on the next page.

ABSTRACT

The use of 4,4-methylenebis (tetrahydro-1,2,4-thiadiazine-1,1-dioxide) in the prevention and control of the development of antibiotic drug resistance in staphylococcus aureus bacteria and in the prevention of bacteria-to-bacteria transfer of genes capable of resisting antibiotics is disclosed.

In The Specification - Clean replacement paragraphs:

Change the third paragraph on page 2 to read in clean form as follows:

Specifically, the present invention relates to the use of 4,4'-methylenebis(tetrahydro-1,2,4-thiadiazine-1,1-dioxide) known generically as taurolidine to treat antibiotic drug (e.g. gentamicin, methicillin and vancomycin) resistant bacterial infections, nosocomial infections and/or eradication of these organisms from an individual acting as a "carrier" for these organisms.

Change the last paragraph on page 2, extending to page 3, to read in clean form as follows:

The development of antimicrobial agents has, without question, been one of the crowning achievements of medical science in the latter half of the twentieth century. However, despite the fact that dozens of classes of compounds have been developed, microorganisms, especially bacteria, have developed resistance to virtually every agent which has been subjected to extensive clinical use. As we approach the end of the twentieth century, there has been a precipitous decline in the development of new antimicrobial agents. There are several reasons for this including the fact that most of the easy targets that allow selective toxicity for antimicrobial agents have been discovered and the fact that it is increasingly expensive to bring a new antimicrobial agent from discovery to the marketplace. There is, however, a major need for discovery of novel classes of antimicrobial agents to which multi-resistant bacteria remain susceptible. Taurolin is such a novel new antimicrobial agent. It has a formulation which comprises taurolidine (4-methylene bis (tetrahydro-1,2,4 thiadiazine 1, 1 dioxide). A derivative of aminosulphonic acid taurineamide, this is a novel bactericidal agent that has a unique specturm

of antimicrobial activity that, in preliminary tests, has include Gram-positive and Gram-negative bacteria and fungi. It has been subjected to early clinical trials and it appears to have useful activity in vivo when administered by intravenous or intraperitoneal routes. This compound also has the ability to neutralize endotoxin in vitro and it also exhibits marked anti-adherence properties in vitro.

Change the second full paragraph on page 10, beginning on line 13, to read in clean form as follows:

As noted above, taurolidine's mechanism of action unlike that of known antibiotics is based on a chemical reaction. While not being bound by any theory, during the metabolism of taurolidine to taurinamide and ultimately taurine and water, methylol groups are liberated which chemically react with the mureins in the bacterial. This results in the denaturing of the complex polysaccharide and liposaccharide components of the bacterial cell wall as well as changing the double standard DNA of the plasmid to a denatured or single stranded DNA.

In The Claims:

Cancel Claims 1-3 without prejudice.

Please insert the following new claims:

4. A method for the prevention of the transfer of plasmid materials containing genes capable resisting the antibiotic vancomycin from a vancomycin resistant strain of bacteria to another, different strain of bacteria comprising administering to a human or other warm blooded animal harboring bacteria containing said plasmid materials an effective amount of the compound 4, 4-methylenebis (tetrahydro-1,2,4-thiadiazine-1,1-dioxide).

5. The method of claim 4 wherein the another, different strain of bacteria is staphylococcus aureus.

6. The method of claim 4 wherein said 4,4-methylenebix (tetrahydro-1,2,4-thiadiazine-1, 1-dioxide) is combined with at least one additional antibiotic.

REMARKS

Claims 1 through 3 have been cancelled. New Claims 4 through 6 have been added.

Note that on July 18, 2001, the undersigned had a telephone conversation with Supervisory Examiner Geist, who agreed that this Divisional Application should be filed to obtain examination and entry of Claims 4-6, as requested in the Amendment mailed by Applicant on March 13, 2001, in Response to the Office Action of December 19, 2000 in the co-pending Application Serial No. 09/265,640.

The foregoing Preliminary Amendment is submitted to correct minor typographical errors appearing in the Application. In particular, the chemical name of the compound taurolidine has been changed to provide that it is a 1,1-dioxide (the Examiner will note that a similar request was made in Applicant's co-pending Application Serial No. 09/266,095).

In addition, a minor change has been made to page 3, line 7, to correct another typographical error, and page 10, line 17 has been amended as requested by the Examiner in paragraph 4 of the Office Action of March 16, 2000 in the Patent Application. It is respectfully submitted that no new matter has been added by the Amendments and entry thereof is deemed proper and is respectfully requested.

New claims 4-6 cover a method for the prevention of the transfer of plasmid materials from a vancomycin resistant strain of bacteria to another, different strain of bacteria by administering taurolidine to a warm blooded animal. Support for new claim 4 can be found in the specification in the paragraph bridging pages 3 and 4 read in conjunction with the paragraph bridging pages 8 and 9 and the first paragraph on page 9 as well as the examples provided in the present Application. Entry of the Amendment is therefore deemed proper and respectfully requested.

Referring to paragraph 6 of the prior Office Action of December 19, 2000, in parent case Serial No. 09/265,640, it is noted that Claim 2 has been provisionally rejected under 35 U.S.C. Section 101 as claiming the same invention as that of claim 2 of co-pending Application No. 09/151,885. Applicants submit that the amendment to the claims is such that new claims 4-6 describe a different invention than that of Applicant's co-pending Application and therefore the double patenting rejection under 35 U.S.C. Section 101 should be withdrawn.

In the prior Office Action of December 19, 2000, in the parent case, Claims 1 and 3 stand provisionally rejected for obviousness type double patenting over claims 1 and 3 of co-pending application No. 09/151,885 and 09/266,215. It is respectfully submitted that these rejections should be withdrawn in consideration of this Preliminary Amendment adding new Claims 4-6, and cancelling Claims 1-3.

Version with markings to show changes made:

ABSTRACT

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Marked-up version of third paragraph on page 2:

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for this including the fact that most of the easy targets that allow selective toxicity for antimicrobial agents have been discovered and the fact that it is increasingly expensive to bring a new antimicrobial agent from discovery to the marketplace. There is, however, a major need for discovery of novel classes of antimicrobial agents to which multi-resistant bacteria remain susceptible. Taurolin is such a novel new antimicrobial agent. It has a formulation which comprises taurolidine [(4~-] (4-methylene bis (tetrahydro-1,2,4 thiadiazine 1, 1 dioxide). A derivative of aminosulphonic acid taurineamide, this is a novel bactericidal agent that has a unique spectrum of antimicrobial activity that, in preliminary tests, has included Gram-positive and Gram-negative bacteria and fungi. It has been subjected to early clinical trials and it appears to have useful activity in vivo when administered by intravenous or intraperitoneal routes. This compound also has the ability to neutralize endotoxin in vitro and it also exhibits marked anti-adherence properties in vitro.

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It is believed that Claims 4-6 are patentable, and in condition for allowance. Accordingly, it is respectfully requested that the claims be examined, allowed, and the case passed to issue.

Respectfully submitted,

Kenneth Watov

Kenneth Watov, Esquire
Registration No. 26,042
Attorney for Applicant

Address All Correspondence to:
Kenneth Watov, Esquire
WATOV & KIPNES, P.C.
P.O. Box 247
Princeton Junction, NJ 08550
(609)243-0330